A DISSERTATION ON

MICROALBUMINURIA
IN
HIV AND AIDS PATIENTS

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CERTIFICATE

This is to certify that this dissertation entitles **"MICROALBUMINURIA IN HIV AND AIDS PATIENTS"** submitted by **Dr. C. RAMESH** to The Tamilnadu Dr. M. G. R. Medical University, Chennai is in partial fulfillment of the requirement for the award of M. D. Degree Branch I (General Medicine) and is a bonafide research work carried out by him under direct supervision and guidance.

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DECLARATION

I **Dr.C. RAMESH** solemnly declare that the dissertation titled **"MICROALBUMINURIA IN HIV AND AIDS PATIENTS"** has been prepared by me. I also declare this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other university, board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the M. D. Degree examination in General Medicine to be held in September 2006.

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INTRODUCTION

Human Immunodeficiency Virus (HIV) infection is spreading through the world in a rampant manner currently. HIV manifests from an asymptomatic carrier state to AIDS. Multiple organs are affected by the invading organism. Renal involvement in HIV patients occurs due to disease per se or due to associated problems like opportunistic infections, septicemia, hypovolemia and drug toxicity[1,2]. HIV infection was recognized in 1980 and the renal pathology of immunodeficiency virus was recognized in 1984 in USA .Renal disorders are encountered at all stages of HIV infection and range from fluid and electrolyte imbalances commonly seen in hospitalized HIV infected patients to HIV associated nephropathy (HIVAN) which can progress rapidly to End Stage Renal Disease [ESRD] [3].

HIV related renal disease have become the third leading cause of end stage renal disease[4]. Overt proteinuria has been encountered in 43-47% of AIDS patients [5]and also low molecular weight proteinuria noticed in over 80% of asymptomatic HIV seropositive patients [6].

Microalbuminuria is an independent and earliest marker of renal damage, and may be the first sign of silent kidney disease. The currently available kidney function test do not identify early kidney involvement. Hence the present study was undertaken to confirm or refute the earlier observations on microalbuminuria in HIV and AIDS cases.

AIM & OBJECTIVES

1. To estimate microalbuminuria in HIV and AIDS patients

2. To correlate the micro albumin level with CD4 cell count.

REVIEW OF LITERATURE

MICROALBUMINURIA

DEFINITION:-

Microalbuminuria has been defined as albumin excretion of 20 to 200 µg/minute (OR) 30 to 300 mg/day in a 24 hours urinary sample, anything above this level of excretion is called macroalbuminuria. Microalbuminuria can also be defined in terms of the urinary albumin to creatinine ratio greater than 30 mg/g in the first voided sample in the morning.

The details are depicted in the table given below.

Table -1

Definition of abnormality in albumin excretion			
Category	**24-hrs Collection (mg/24hrs)**	**Timed Collection (µg/min)**	**Spot collection (mg/g cre)**
Normal	< 30	< 20	< 30
Microalbuminuria	30 – 299	20 - 199	30 – 299
Clinical albuminuria	≥300	≥200	≥300

PATHOPHYSIOLOGY OF MICROALBUMINURIA

The glomerular capillary wall (GCW) provides a barrier to filtration of large macromolecules. The GCW has 3 components

i) Endothelium of the capillary

ii) Basement membrane

iii) Epithelial cells (podocytes). Surrounding the outer surface of the capillary basement membrane .

Together, these make up the filtration barrier, which despite the three layers, filters several hundred times as much water and solutes as the usual capillary membrane. The barrier to filtration is provided by 2 mechanisms**:** **size selectivity and charge selectivity.**

Filterability of substances by glomerular capillaries decreases with increasing molecular weight.

Filterability of selected substances is shown in Table2.

Table- 2

Substance	Molecular Weight	Filterability
Water	18	1.0
Sodium	23	1.0
Glucose	180	1.0
Myoglobin	17000	0.75
Albumin	69,000	0.005

Size selectivity is a feature of the size of the pores in the components of the barrier. The endothelial cells have fenestrations with an approximate radius of 40nm and, as such, do not provide an effective barrier to albumin, which has a radius of 3.6 nm. The GBM has pores with a radius of 4 nm. Between the foot processes of epithelial cells, a thin membrane called a slit diaphragm provides a barrier to filtration. The pores in the slit membrane are the same size as those in the GBM. The GBM and slit diaphragms are, therefore, the major components of size selectivity.

Charge selectivity is provided by negatively charged anions, such as heparan sulphate proteoglycan , which repel negatively charged molecules such as albumin. These anions are present on both endothelial cells and the GBM, which thus provide charge selectivity. The negative charge on the GBM also may be important for adhesion of epithelial cells , such that loss of the negative charge may result in disruption of the epithelial cell barrier, which in turn contributes to increased permeability to macromolecules such as albumin (due to loss of size selectivity). When damage to the basement membrane or components of the glomerular epithelial cell occur, often the first manifestation is the appearance of plasma proteins in the urine.

Because albumin is the major circulating protein in plasma and is relatively close in size to that of the size selectivity barrier, its appearance in the urine is the most sensitive indicator of damage or disruption of the glomerular filtration barrier.

HUMAN IMMUNODEFICIENCY VIRUS

The origin of HIV is unclear. The most likely scenario is that HIV was introduced into human from another primate in sub Saharan Africa. [7]

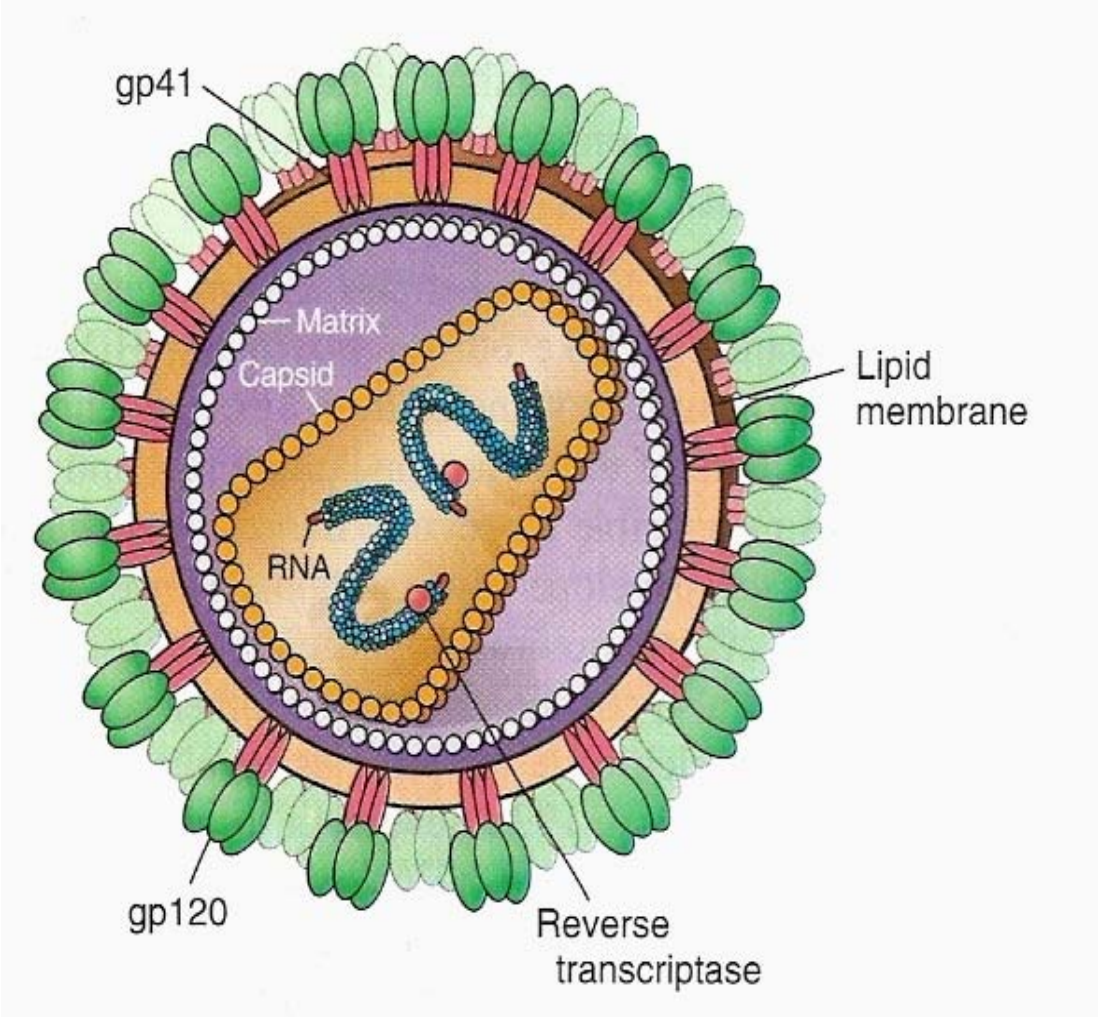
ETIOLOGY AGENT :-

The etiologic agent of AIDS is Human Immuno deficiency Virus1 (HIV-1) & HIV-2 belongs to the family of human retroviruses (Retroviridae) and the subfamily of lentiviruses .

MORPHOLOGY OF HIV :-

Electron microscopy shows that the HIV is spherical enveloped virus, about 90-120 nm in size. The nucleocapsid has an outer icosahedral shell containing numerous external spikes formed by the two major envelope proteins, the external gp 120 and the transmembrane gp 41, and an inner cone shaped core , enclosing the ribonucleproteins.

ELECTRON MICROSCOPIC VIEW OF HIV



ATTACHMENT AND ENTRY

The replication cycle of HIV begins with the high affinity binding of the gp 120 protein via a portion of its v1 region near the N terminus to its receptor on the host cell surface , the CD4 molecule . It is also expressed on the surface of monocytes / macrophages and dendritic / langerhans cells . Once gp 120 binds to CD4, the gp 120 undergoes a conformational change that facilitates binding to one of a group of co – receptors . The two major co–receptor of HIV -1 are CCR5 and CXCR4.

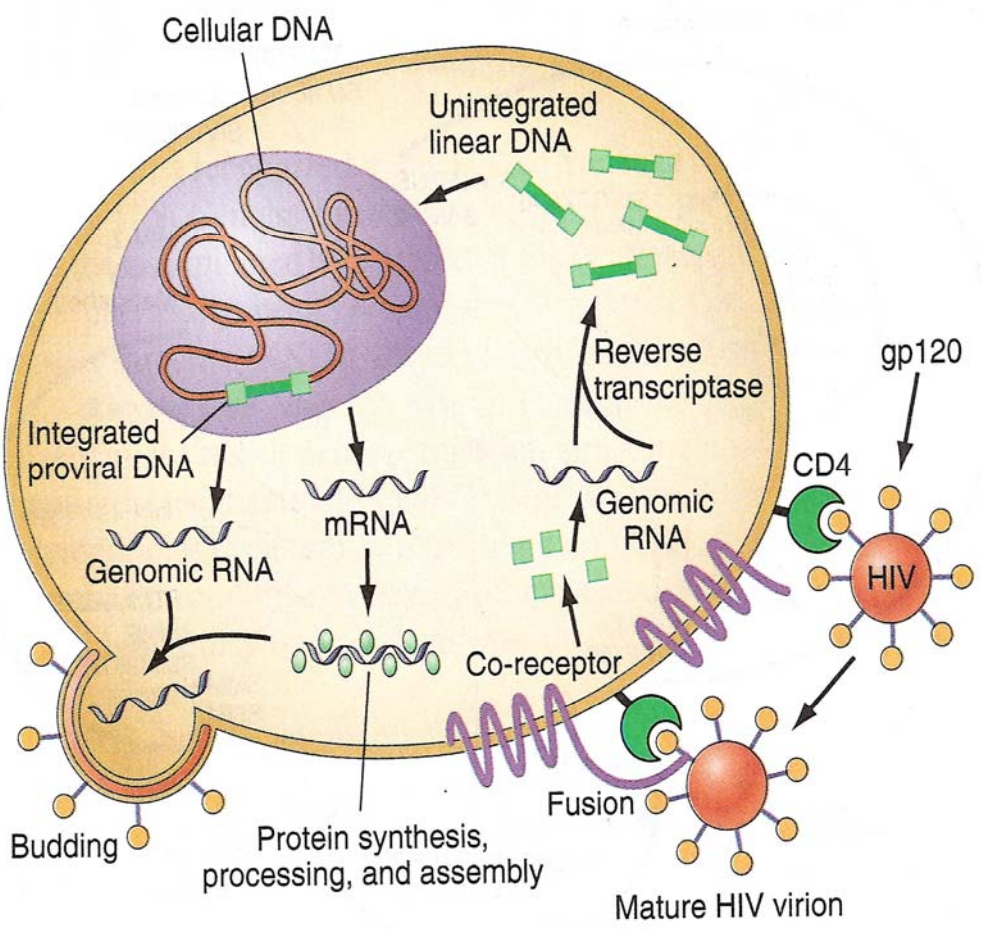
REVERSE TRANSCRIPTION AND INTEGRATION

Following binding of the envelop protein to the CD4 molecule, the virus is "uncoated " and the viral RNA is converted into complementary DNA (C-DNA) by vireon – associated reverse transcriptase enzyme . The C-DNA is transported to the host cell nucleus and eventually gets incorporated into the host cell chromosomes. Virus specific **integrase** enzyme is essential for this function.

TRANSCRIPTION , TRANSLATION AND REPLICATION

The integrated DNA is transcribed into messenger RNA (mRNA) which comes out into the cytoplasm and viral proteins are synthesized using protein synthesizing machinery and raw material from the host cell . Some of the viral proteins are synthesized as polyproteins that are eventually cleared by protease enzyme.

REPLICATION CYCLE OF HIV



MATURATION AND RELEASE

Newly synthesized progeny RNA and proteins are packaged together and the newly formed virus particles are released from the infected cell by the "budding" process .

HIV GENOME

HIV-1 has the following genes, gag – encodes the proteins that form the core of the virion. Pol – encodes the reverse transcriptase enzyme. env – for envelope glycoproteins. It also contains atleast six other genes tat , rev, nef, vif, vpr and vpu, which code for proteins involved in the regulation of gene expression.

The major difference between the genomes of HIV 1 and HIV 2 is the fact that HIV 2 lacks the vpu gene and has a vpx gene not contained in HIV-1.

EPIDEMIOLOGY:-

India is now considered the country with largest number of infected persons in the world [8]. India alone accounts for 4 million cases. The spread mainly occurs through heterosexual route.

PATTERN OF HIV TRANSMISSION

Table - 3

Type of exposure	% of global total	Efficiency per single Exposure	% of India total
Sexual inter course Vaginal Anal	 70-80% 5-10%	 0.1-1% 0.1-1%	83.3%
Perinatal	5-10%	30%	2%
Injection drug use	5-10%	0.5-10%	3.8%
Blood Transfusion	3-5%	>90%	3.5%
Health care Needle sticks	<0.01	<0.5	

MOLECULAR EPIDEMIOLOGY OF HIV

According to DNA sequence data HIV-1, can be divided into three major groups .

1. Group 'm' (major), which contains ten genetically distinct sub types - A to J.
2. Group 'O' (outlier), which contains various heterogeneous viruses .
3. Group 'N' (Cameroon type)

In addition, there are at least 5 sub types of HIV-2, it is the predominant virus in West Afican countries and has also been reported in India. Importance of molecular epidemiology is that it can offer clues as to how the virus spreads between the regions and continents.

PROGRESSION OF ILLNESS:-

Average period to develop AIDS is 8 – 10 yrs. The documented cytopathic effect is 50-80 cells/μL per year. About 5-10% of infected people progress to AIDS with in 2-3 years, they are called rapid progressors. About 5% of infected people do not progresses to AIDS even after 10 years, they are called long term non progressors.

The reasons being

1. Mutant nef gene of HIV [9]
2. Defective CCR-5 co binding protein on macrophage due to genetic abnormality in the patient [10]

CLASSIFICATION

Revised classification system for HIV infection and expanded AIDS surveillance case definition for adolescents and adults (CDC –Atlanta)-1993.

Table- 4

CD4 + Cell count (per microlitre) Conditions	**CLINICAL CATEGORIES**		
	A	**B**	**C**
	Asymptomatic, acute primary infection or PGL	Symptomatic but not A or C conditions	AIDS indicator
>500	A1	B1	C1
200 – 499	A2	B2	C2
<200	A3	B3	C3

PGL - Progressive Generalized Lymphadenopathy

HIV infected persons classified in A3, B3, C1,C2,C3 are AIDS cases.

1993 AIDS surveillance case definition CDC Atlanta:

Category A:

One or more of the following conditions in an adolescent (>13 years of age) or adults

1. Asymptomatic HIV infection
2. Progressive Generalized Lymphadenopathy
3. Acute (Primary) HIV infection with accompanying illness or history of acute HIV infection.

Category B:

Consists of symptomatic conditions in an HIV infected adolescent or adult that are not included in clinical category'C' and that meet at least one of the following criteria.

a) The conditions are attributed to HIV infection or indicative of a defect in cell mediated immunity (CMI).
b) conditions are considered by physician to have a clinical course or to require management that is complicated by HIV infection.

Examples include

1. Bacillary angiomatosis
2. Vulvo vaginal candidiasis (Persistent , frequent or poorly responsive to therapy) oral candidiasis
3. Cervical dysplasia, cervical carcinoma in situ
4. Constitutional symptoms lasting more than one month
5. Oral hairy leukoplakia
6. Herpes zoster involving at least 2 distinct episodes or more than one dermatome
7. Idiopathic thrombocytopenic purpura
8. Listeriosis
9. Pelvic inflammatory disease
10. Peripheral neuropathy

Category 'C':

AIDS Indicator Conditions:

1. Candidiasis of the bronchi, trachea or lungs
2. Oesophageal candidiasis
3. Cervical cancer – invasive
4. Coccidioidomycosis - disseminated or extrapulmonary
5. Cryptococcosis – extra pulmonary

6. Cryptosporidiosis – Chronic intestinal (> one month duration)
7. Cytomegalovirus disease (other than lung, spleen and nodes)
8. CMV retinitis (with loss of vision)
9. HIV related encephalopathy
10. Herpes simplex – chronic ulcer, bronchitis, pneumonia or oesophagitis
11. Histoplasmosis – disseminated or extra pulmonary
12. Isosporiasis – chronic intestinal (> one month duration)
13. Kaposi's sarcoma
14. Burkitt's lymphoma
15. Immunoblastic lymphoma
16. Primary brain lymphoma
17. MAIC, M.kansasii infection– disseminated or extra pulmonary
18. M.tuberculosis – any site
19. Mycobacterium other species or unidentified species - disseminated or extrapulmonary
20. Pneumocystis Jiroveci pneumonia
21. Recurrent pneumonia
22. progressive Multifocal Leukoencephalopathy
23. Salmonella septicaemia – recurrent
24. Toxoplasmosis of brain
25. Wasting syndrome

RENAL INVOLVEMENT IN HIV AND AIDS

Historical perspective

Rao et al[11], in 1984 described focal and segmented glomerulosclerosis in nine patients with AIDS and nephritic syndrome . The changes were similar to heroin induced nephropathy, the progression to end stage renal disease in these patients was much more rampant. In the same year pardo et al [12], reported a variety of glomerular changes seen at autopsy in patients with AIDS. Since then many reports have validated renal involvement in HIV infected population and a wide spectrum of renal syndromes have been reported .

Spectrum of renal diseases

The renal manifestation of HIV infection occur commonly during all stages of infection[3]. Renal manifestations of HIV infection occurs in 6 – 10 % of HIV seropositive individuals.[13] A wide spectrum of renal syndromes has been associated with HIV infection.

Overview of HIV related renal diseases

Acute renal failure

Pre renal

- ♦ Hypovolemia

  [Diarrhoea, vomiting, bleeding, pancreatitis]

- ♦ Hypoalbuminemia

  [severe malnutrition , cirrhosis]

Renal

Mostly induced by drugs

- ♦ Acute tubular Necrosis

  [Aminoglycosides, amphotericin B, foscamet, pentamidine,

  contrast based dyes, rhabdomyolysis]

- ♦ Allergic interstitial nephritis

  [protease inhibitors, trimethoprim /sulfamethaxazole,

  phenytoin cephalosporins]

- ♦ Crystal deposition [protease inhibitors, sulfadiazine, acyclovir]

Post Renal

- ♦ External obstruction

  [Tumor, prostate hyperplasia, urethral obstruction,

  retroperitoneal fibrosis]

- ♦ Internal obstruction [crystal deposition, blood clots,

  tumor lysis]

B) Chronic Renal failure

Focal glomerulosclerosis (classic HIVAN)

Immune complex disease

- ♦ IgA nephropathy
- ♦ mixed sclerotic immune complex nephropathy
- ♦ proliferation glomerulo nephritis

Microangiopathies

- ♦ Hemolytic uremic syndrome
- ♦ Thrombotic thrombocytopenic purpura

Renal amyloidosis

Renal paranchymal invasion by malignancies

[lymphoma , Kaposi's sarcoma]

C) Fluid and electrolyte disorders

Hyponatremia due to

- ♦ fluid loss
- ♦ SIADH
- ♦ Infection – toxoplasmosis , tuberculosis , pneumocystis
- ♦ Adrenal insufficiency

Hyprerkalemia due to

- ♦ Adrenal insufficiency
- ♦ Hyporeninemic hypoaldoteronism
- ♦ IDDM [pentamidine induced, pancreatic cell dysfunction]
- ♦ severe ARF

Hypokalemia due to

- ♦ GI losses
- ♦ Renal potassium wasting

Metabolic alkalosis due to

- ♦ Upper GI loss
- ♦ Hypokalemia

Metabolic acidosis due to

- ♦ Renal failure
- ♦ Septic shock
- ♦ Diarrhoea
- ♦ Drug induced interstitial nephritis

ACUTE RENAL FAILURE

The fundamental etiology and mechanisms involved in acute renal injury in HIV patients are generally the same as in non HIV patients. Acute deterioration in renal failure may be thought of as pre renal, intrinsic to renal tissue and post renal. In over whelming number of patients with ARF, pre renal etiology is noted. Pre renal causes of ARF include hypovolemic states due to profuse vomiting, diarrhoea and infections, sepsis, excessive and life threatening bleeding .

Intrinsic ARF in HIV infected patients may be due to hypovolemic, sepsis, shock and use of nephrotoxic agents for therapeutic and diagnostic purposes. Rhabomyolysis, azotemia, use of NSAIDS, hemolytic uremic syndrome (HUS) and thrombocytopenic purpura (TTP) are the other causes of ARF .

Post renal acute renal failure may be either due to extra renal or distal obstruction, intrinsic obstruction may also lead to post renal ARF. Out flow obstruction , retroperitoneal fibrosis and crystalluria may contribute to post renal ARF. Indinavir , sulfadiazine and acyclovir have been implicated in crystalluria . [14]

Acute renal failure classified as mild ARF and severe ARF

Mild ARF :-

Defined as a peak sr.creatinine of >2 mg/dL and occurs upto 20% of hospitalized HIV infected patients .[15]

Severe ARF :-

Defined as a peak sr.creatinine of > 6 mg/dL seen in 75% of cases. Severe renal failure in HIV infected patients may be associated with terminal conditions in which acute dialysis would be inappropriate.

FLUID & ELECTROLYTE DISORDERS :-

Among the electrolyte abnormalities observed in HIV patients , hyponatremia and hyperkalemia are most significant.

Hyponatremia:-

- It is the most common, reported 30 – 60% of hospitalized symptomatic HIV and AIDS patients .
- Severe hyponatremia in HIV infected patients [16] indicate poor prognosis
- Volume depletion due to diarrhoea or vomiting is the usual cause of hyponatremia present at the time of hospital admission.
- Excess body water is attributed either to hypovolemia with physiologic stimulation of ADH, administration of hypotonic fluids or the SIADH.

SIADH is the likely culprit in those who develop hyponatremia during hospitalization [15] .

- SIADH is usually associated with common pulmonary and intracranial disease such as pneumocystis pneumonia, toxoplasmosis, tuberculosis.
- AIDS patients have a high incidence of adrenal abnormalities. Adrenal pathology particularly CMV infection is found common in patients who have died from AIDS.[17] Other pathologic lesions that have been noted frequently include hemorrhage toxoplasma infection, Cryptococcus, mycobacterium tuberculosis , MAC , infiltration with Kaposi's sarcoma and lymphoma .

Hyperkalemia :-

Occurs as a result of the effect of

- High dose of trimethoprin – sulfamethoxazole or IV pentamidine. The underlying mechanisms with both drugs consists of inhibition of distal nephron sodium transport, leading to a decrease in distal potassium secretion. [1] Trimethoprin shares structural similarity with the potassium sparring diuretic triamterene.
- Hyperkalemia and hyponatremia may also be manifestation of minerlo corticord deficiency due to adrenal insufficiency or the syndrome of hyporeninemic hypoaldosteronism .[18]

- A systemic abnormality in potassium equilibrium, which favours the development of hyperkalemia by a mechanism unrelated to renal potassium excretion, has been identified in HIV infected patients individuals. [19]

III **CHRONIC RENAL FAILURE**

a) HIV associated nephropathy (HIVAN)

HIVAN represents a major complication of HIV infection. The evolution of HIVAN is the development of nephrotic syndrome initially and progress to end stage renal disease in most patients.[20]

HIVAN has become the most common single diagnosis in HIV infected patients with renal insufficiency. The true prevalence of HIVAN is not known. HIVAN is common in urban centers with prevalence of about 10%. The geographic distribution of HIVAN is not uniform and depends on specific risk factors which include race, gender and drug use.

HIVAN is recognized throughout the spectrum of HIV disease . It can be first manifestation of HIV infection or even precede detection of HIV andibodies.[21]

HIVAN is 7–10 times more common in men, men comprises 80 to 90 % of cases [22], Black men have increased risk. 30 – 60 % of people with HIVAN have a history of Intra Venus Drug Users (IVDU).[23] The remainders are either homosexual or originate from regions where HIV infection is endemic. In approximately 10% patients no specific risk factors for HIV can be identified.

Unfortunately, most patients who develop HIVAN do not have early signs or symptoms that would provide a clue to this diagnosis prior to the onset of progressive nephropathy.

PATHOGENESIS :-

The pathogenesis of HIVAN has been studied intensely over the past 15 years. The question in the pathogenesis of HIVAN is whether the disease can be attributed to direct viral effect or to HIV related changed on the cytokine milieu. HIVAN is caused by HIV gene expression in renal tissue, resulting in injury of glomerular and tubular epithelial cells.

Early studies using in situ hybridation to a C-DNA nuclei acid probe found the HIV genome in tubular and glomerular epithelial cells in patients with HIVAN. Patients with immune mediated glomerulonephritis or HIV infected patients with no renal disease had less cellular involvement.

Since HIV proliferation appears to be the major determinant of cytotoxicity, factors that precipitate viral replication with in the kidney could explain the sudden onset of the disease. HIV proliferation is regulated by at least two genes **nef and vif** with opposing action. Minor mutation in either of these could lead to rapid viral proliferation and death of the host cell. Concomitant infection with viral hepatitis, syphilis or CMV, could induce HIV replication. CMV may promote viral proliferation, through a mechanism that is dependant on tumor necrosis factor (TNF). [24]

HIV is a potent stimulation of transforming growth factor β a cytokine strongly implicated in the development of fibrosis. The transgenic mouse model (Tg 26) suggests that activation of the cytokine could will be the basis for the extensive interstitial fibrosis and glomerularsclerosis that are the hall marks of HIVAN.[25]

HIV DNA and protein markers specific for HIV has been demonstrated in tubular epithelium, glomerular epithelial cells and mesangeal cells by a variety of techniques in vitro and in renal biopsy tissue of HIV patients.[26]

In transgenic mouse model (Tg 26) HIV-1 envelope (gp 41 and gp 120) and regulatory genes are expressed but gag and pol genes are deleted to render the virus non infections. These mice develop a syndrome closely resembling HIVAN.[27] Kidneys were transplanted between normal and transgenic mice. HIVAN then developed in the non transgenic littermates, where as the normal kidneys remained disease free when transplanted into transgenic littermates. This study provides evidence that HIVAN is caused by a direct HIV gene expression rather than the systemic effects of HIV infection . [28]

HIV infection may involve epithelial cells from multiple segments of the nephron, including proximal tubule, thick ascending loop of Henle and collecting duct. This pattern of involvement may explain the tubular dilatation seen in kidney biopsy specimens of patients with HIVAN .[29]

The kidney also seems to be a reservoir for HIV. Despite undetectable viral levels in the serum, a case report described a patient who continued to express HIV in renal epithelial cells determined by RNA in situ hybridation.[30] There is also compelling evidence that active replication of HIV occurs in kidney epithelium, possibly producing HIV strains in the kidney microenvironment, that differ from HIV circulating in the blood. This suggest that kidney may serve as a viral reservoir

harboring HIV strains that have evolved under tissue, specific selection pressures.[31]

HISTOPATHOLOGY :-

HIVAN is associated with characteristic glomerular tubulo interstitial and ultra structural lesions. Autopsy data demonstrates that 90% of patients with the clinical diagnosis of HIVAN have focal and segmental glomerulosclerosis.[16]

Histopathologically, classic HIVAN is a collapsing form of focal segmental glomerulosclerosis with podocyte hyperplasia and dedifferentiation, associated with severe tubulopathy which is characterized by tubular apoptosis, microcytes and interstitial fibrosis.[32]

Light microscopic features :-

- Collapsing focal segmented glomerulosclerosis or masangial hyperplasia.
- Cystic tubular dilatation
- Interstitial edema
- Cellular infiltration by lymphocytes or monocytes
- Dilated degenerating proximal tubules filled with eosinophilic material, possible representing cast formation in situ.

Electron microscopy features:-

- The presence of numerous tubuloreticular inclusions with in endothelial cells is important finding in HIVAN. Finding numerous tubuloreticular inclusions in capillary endothelial cells in a patient with FSGS prompts some pathologists to request HIV antibody testing [HR enuka , Brigham and women's hospital , personal communication, 1994] .
- Although renal tissue may stain for IgM, c1q, c3 and kappa or lamda light chains in areas of focal sclerosis, immunologic mechanisms are probably not central to genesis of HIVAN.[33]

CLINICAL PRESENTATION

- ♦ Proteinuria but no hematuria on urine analysis
- ♦ High grade proteinuria usually in nephrotic range(>3.5 gms/day) Proteinuria is the hallmark of HIVAN. Over all microalbuminuria is seen in ~20% of untreated HIV infected patients, significant proteinuria is seen in 2%.[34]

INVESTIGATION:-

- ♦ Urine analysis often reveals severe proteinuria with oval fat bodies and frank lipiduria, Broad waxy casts also seen.
- ♦ Microalbuminuria is seen in ~20% of untreated HIV patients.

- ♦ Azotemia, proteinuria or both are the presenting feature in >90% of HIV infected patients.
- ♦ Renal ultrasound: shows normal or enlarged renal silhouette with increased echo genicity .

Renomegaly may be the result of

a) in sufficient time for global sclerosis and fibrosis in the rapid progression of renal disease.

b) marked dilation of the tubules with numerous microcyts, in contrast to the tubular collapse frequently seen in other forms of chronic renal injury and interstitial edema.[35]

- ♦ Renal Biopsy :- confirm the clinical diagnosis of HIVAN.

MANAGEMENT:-

The rate of progression from the initial presentation to ESRD was 2.5 months in the pre HAART. HAART therapy has been shown to retard the progression of renal disease in persons with HIVAN.[36]

Available treatments are

- ♦ Anti retroviral therapy
- ♦ steroid treatment
- ♦ ACE inhibitors

ART :-

There have been case reports of dramatic improvements in renal function with initiation of combination ART[30] but no prospective studies have shown a benefit in the course of HIVAN. Most reports experience is with zidovudin may slow or reverse the rapid deterioration associated with HIVAN.[37]

Steroid treatment :-

There is 20 to 40 response rate to corticosteroids therapy. Prednisolone 60 mg/day for 2 to 11 weeks leads to a significant reduction in sr.creatinine and 24 hrs urine protein excretion [38] due to reversal of interstitial inflammation and 80% reduction in risk of progressive azotemia.[39]

ACE inhibitors:

Angiotension II increases the cellular synthesis of transforming growth factor beta (TGF β) which has been implicated in the pathogenesis of HIVAN, ACE inhibitors are effective in slowing the progression of renal insufficiency by reducing production TGF β in both humans and HIV transgenic mice. Studies suggest that ACE inhibitors

Initiated early may offer renal survival benefits in HIVAN.[40] Renal biopsy should be offered to patients as the treatment implications and prognosis vary according to the biopsy results .

Risk factors for progressive renal disease include

- ♦ CD4 cell count <200 cells / μl.
- ♦ Detectable HIV RNA level
- ♦ Hypertension
- ♦ Hypo albuminemia
- ♦ Elevated Sr.creatinine[41]

II) Immune complex Disease

HIV associated immune mediated renal disease in the most common glomerular disease found on renal biopsy in series reported from Italy and France.[22]

Important forms of immune complex GN in HIV infections are

i) IgA nephropathy

ii) Hepatitis C virus related renal disease.

HIV has been implicated as a stimulus for immune complex formation in IgA nephropathy, immune complexes with antigen have

been identified in the circulation and renal tissue eluates of HIV infected patients with IgA nephropathy and with other immune complex GN.[42]

Other patterns of glomerular involvement are

- ♦ membranous nephropathy
- ♦ membrane proliferation GN
- ♦ mesangial proliferation GN
- ♦ Diffuse proliferation GN
- ♦ cresentic GN

III) Microangiopathies associated with HIV infection may present as hemolytic uremic syndrome or thrombotic thrombocytozenic purpura .

Other renal diseases reported less commonly

- ♦ Minimal change disease
- ♦ Amyloidosis
- ♦ Tumor invasion of the kidneys

END STAGE RENAL DISEASE

HIVAN has become the third leading cause of ESRD among African Americans aged 20 – 64 years.[43] Black patients infected with HIV are at risk for the development of HIV ESRD, irrespective of mode of viral acquisition.[44]

Management options for these patients include

- ♦ Hemodialysis
- ♦ Peritoneal dialysis
- ♦ Transplantation

MICROALBUMINURIA IN HIV AND AIDS PATIENTS

Microalbuminuria is the earliest marker for the renal involvement. Overall, microalbuminuria is seen in ~ 20% of untreated HIV infected patients.[34] Significant proteinuria is seen in 2%. Various studies were conducted to find out the incidence of microalbuminuria in HIV infected patients.

LUKE et al,[45] noticed abnormal urinary levels of micro albumin in 19.4% of HIV positive patients. Micro albumin levels were not correlated with race, sex, risk factor of AIDS, disease history or concurrent drug therapy .

In contrast, urinary micro albumin levels were correlated with CD4 T cell, suggesting an association between AIDS progression and microalbuminuria .

Busch et al,[46] study also found that albuminuria occurred exclusively with CD4 T cell counts below 200 / mm3.

Despite of available literature on this area, no such work has been carried out in this part of the country with local AIDS cases due to inherent constraints. This study attempts to fill up the gap.

MATERIALS AND METHODS

Setting : This study was carried out at Government Rajaji Hospital, Madurai Medical College, Madurai.

Collaborating Department : Anti retroviral therapy centre / Sexually transmitted disease Dept and Nephrology department Madurai Medical College, Madurai.

Study Design : Cross sectional study

Period of study: Dec 2004 to Dec 2005

Sample size & Selection of study subjects:

The study was conducted in HIV positive patients who were attending the ART clinic, Government Rajaji Hospital, Madurai. 300 HIV positive patients were screened, of which, 60 patients who satisfied the inclusion criteria included in the study and further evaluated. 20 healthy individuals (age and sex matched) were kept as control.

Inclusion criteria :

Adult male & non pregnant female HIV infected AIDS patients before ART therapy.

Exclusion criteria :

Children, overt renal disease, Diabetes mellitus , systemic hypertension, collagen vascular disease, cardiomyopathy, urinary tract infection and Nephrotoxic agents used patients.

Ethical issues :

The study group thus identified by the above criteria (inclusion & exclusion) are first briefed about the nature of the study . Willing participants were taken up after getting a written informed consent from them.

Materials :

Total of 60 cases who satisfied the inclusion & exclusion criteria above were taken up for the study . Twenty age and sex matched subjects were kept as control.

Conflict of interest : There was no conflict of interest .

Financial support : NIL.

LIMITATION

1. Due to technical and financial constraints, only 60 cases and 20 controls could be measured for microalbuminuria.
2. Only microalbuminuria & 24 hours urinary protein was measured.
3. Renal biopsy was not attempted due to ethical reason.
4. Long term follow up was not attempted.
5. Effect of ART on microalbuminuria was beyond the purview of the study.
6. Viral load could not be estimated due to constraints.

METHODOLOGY

Selected socio-demographic , clinical , and laboratory data were elicited from the patients and controls and recorded in a proforma.

I . Socio- demographic data:

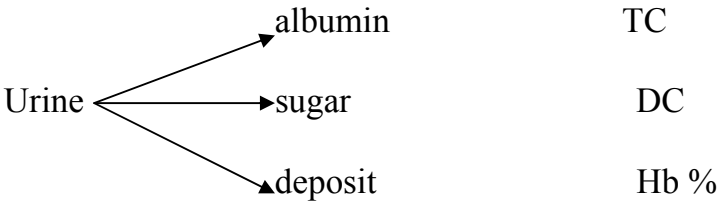
Age

Sex

II . Clinical data :

Clinical examination

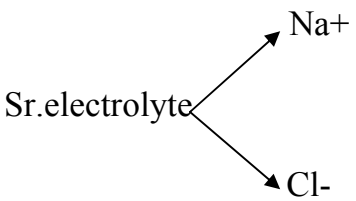
III . Laboratory data :



Bl.sugar

Bl.urine

Sr.creatinine



Microalbuminuria & Urine albumin / creatinine ratio :-

Here the 24 hours urine was collected. It is measured by radio immuno assay for microalbuminuria & Urine albumin / creatinine ratio.

24 hours urinary protein

CD4 count :

The standard method for enumerating CD4 T cells uses a flow cytometer. A computer calculates the number of CD4 T cells by analyzing the size of the cell and which of the antibodies it has been tagged with. The overall process is called Fluorescence Activated Cell Sorting (FACS)

ECG

USG abdomen

IV . Statistical analysis :

Data was entered in Microsoft excel spread sheet and analyzed, statistically using standard statistical software. Student 't' test and chi-square test were applied for significance. Significance was considered if the 'p' value was below 0.05.

RESULTS

The total number of subjects included in this study was 80. Among these 80 subjects, 60 were case (HIV and AIDS patients) and 20 were controls.

Table- 5

Distribution of case & control : Age wise

Age group	**Cases**		**Control**	
	NO	%	NO	%
21 – 30	22	36	9	45
31- 40	30	50	9	45
41- 50	8	14	2	10
Total	60	100	20	100
Mean age	33.57		31.8	
SD	5.94		6.87	

This table compares the mean age of cases and controls. There is no significant difference between the cases and controls with respect to age.

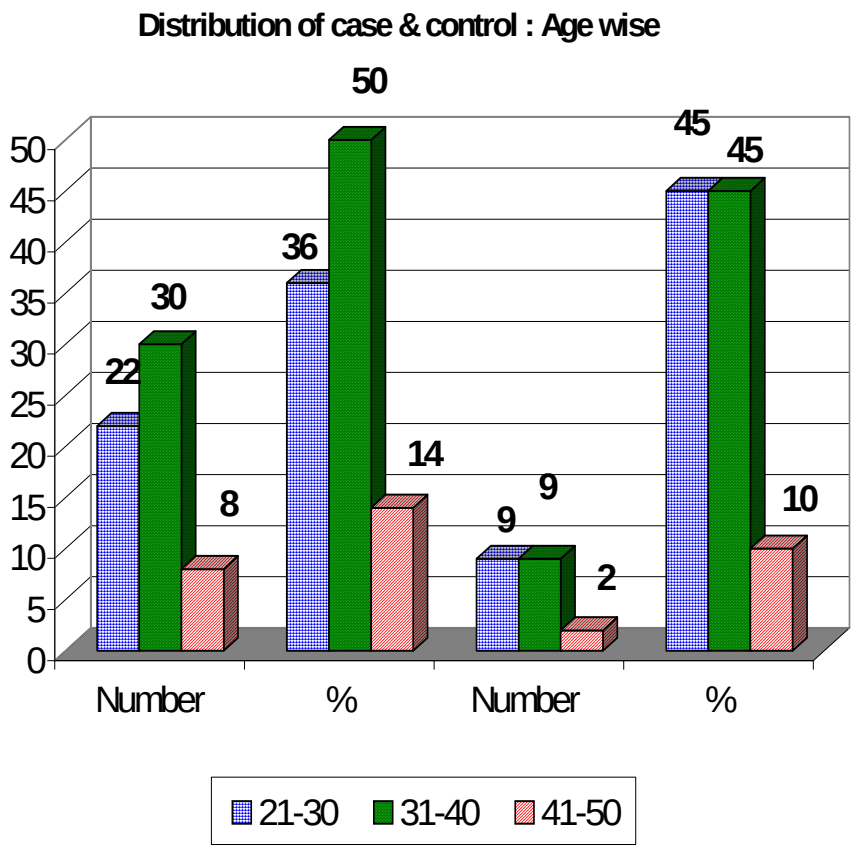

Distribution of case & control : Age wise
50
45
40
35
30
25
20
15
10
5
0
22
30
8
36
50
14
9
9
2
45
45
10
Number
%
Number
%
21-30
31-40
41-50

Table -6

Distribution of cases and control : gender wise

Sex	Cases		Controls	
	NO	%	NO	%
Male	31	51.7	10	50
Female	29	48.3	10	50
Total	60	100	20	100

The table compares the sex distribution in cases and controls . There is no significant difference in the distribution with respect to sex.

Distribution of cases and control : Gender wise

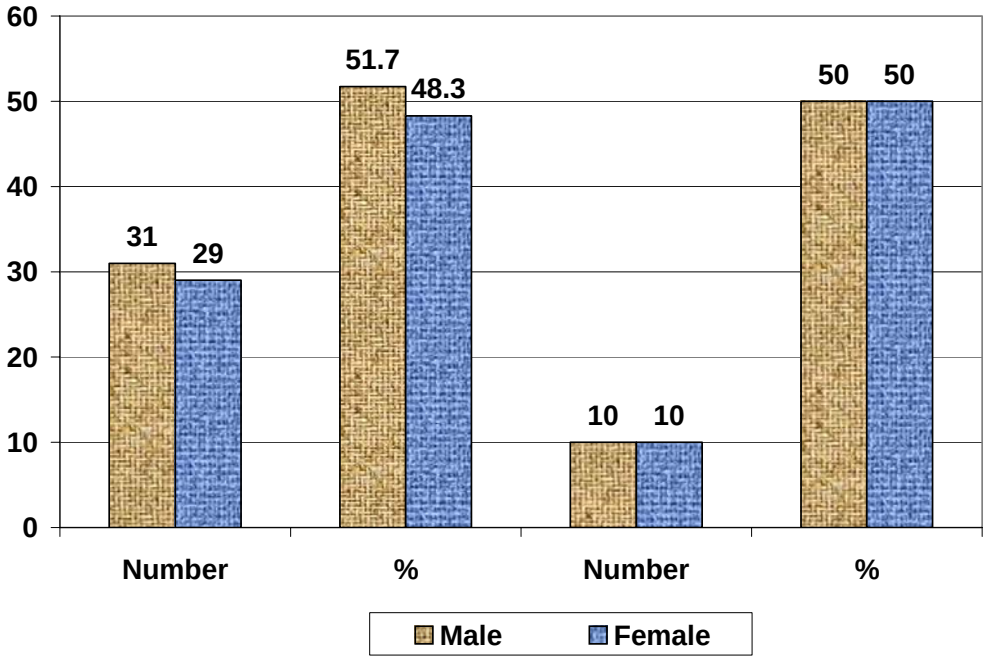


Table -7

Case distribution in relation to CD4 count.

CD4 count	No of cases
Group A CD4 < 200	30
Group B CD4 >200	30

The cases are equally divided into 2 groups, based on CD4 counts, in patients group A has CD4< 200, group B has CD4 > 200, each group consists of 30 members.

Table- 8

Distribution of cases in relation to CD4 Count : Age & Gender wise

	Group A CD4 <200		**Group B CD4>200**	
AGE	Male	Female	Male	Female
21-30	7	4	2	9
31-40	7	7	12	4
41-50	1	4	2	1
Total	15	15	16	14

p value for Sex = 0.7961

p value for Age = 0.6164

This table shows there is no significant difference in the CD4 count with respect to age and gender.

Distribution of cases in relation to CD4 Count : Age & Gender wise

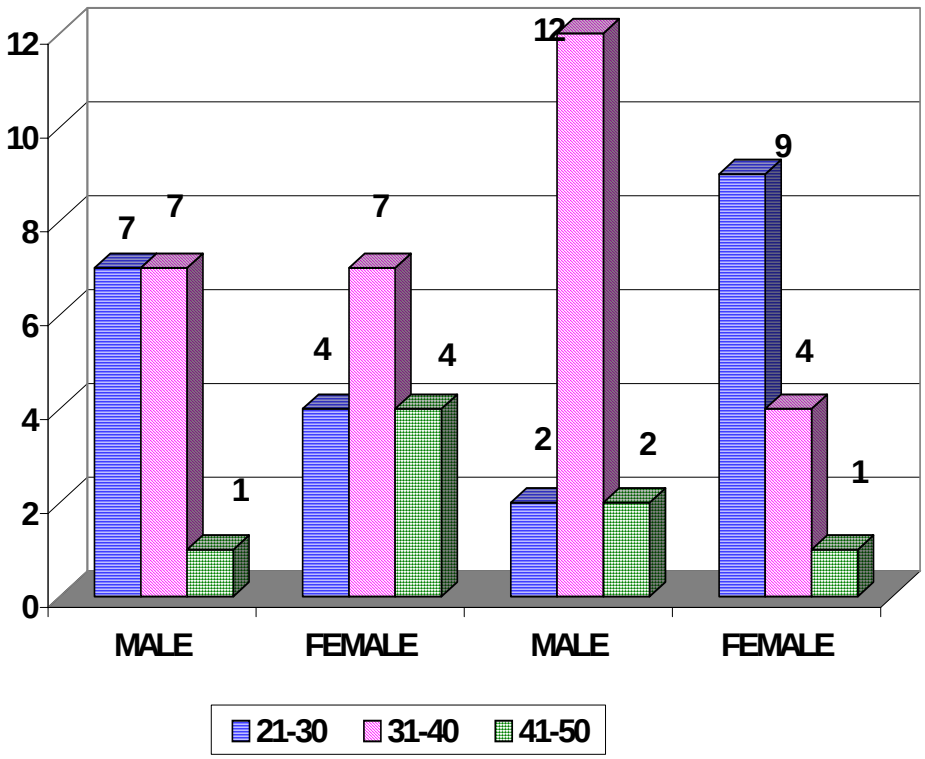


Table - 9 A

Microalbuminuria between cases and controls

	Cases		**Controls**	
	No	%	No	%
Microalbuminuria	16	26.6	Nil	0
Normal	44	73.4	20	100
Total	60	100	20	100

This table shows 26.6% of cases had microalbuminuria and none of the controls had microalbuminuria.

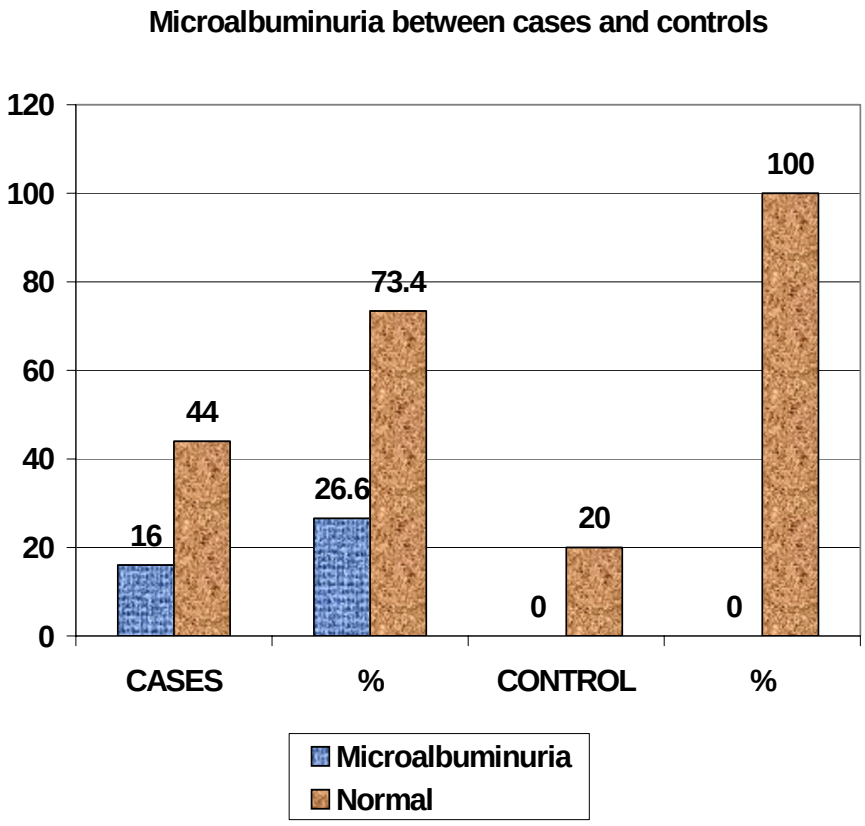

Microalbuminuria between cases and controls
120
100
80
60
40
20
0
16
44
26.6
73.4
0
20
0
100
CASES
%
CONTROL
%
Microalbuminuria
Normal

Table - 9 B

	Cases		Controls	
Microalbuminuria	Mean	SD	Mean	SD
	31.14	34.34	2.93	2.68

Using students 't' test = 6.31

P value < 0.000001.

The mean microalbuminuria is 31.14mg/day (SD 34.34) in cases and 2.93 mg/day (SD 2.68) in controls. P value < 0.000001, this clearly shows microalbuminuria level is significantly higher in HIV and AIDS patients.

Table – 10

Distribution of microalbuminuria in cases :- Age & Gender wise

	GROUP A CD4 < 200		GROUP B CD4 > 200	
Age	Male	Female	Male	Female
21-30	3	1	-	1
31-40	3	5	-	-
41-50	1	1	1	-
Total	7	7	1	1

In group A, with CD4 count < 200, Microalbuminuria is seen in 14 cases, comprising 7 male and 7 female patients.

In Group B, with CD4 count > 200, Microalbuminuria is seen in 2 cases, comprising 1 male & 1 female patient.

The table shows microalbuminuria not affected by the gender.

Distribution of microalbnuminuria in cases Age& Gender wise

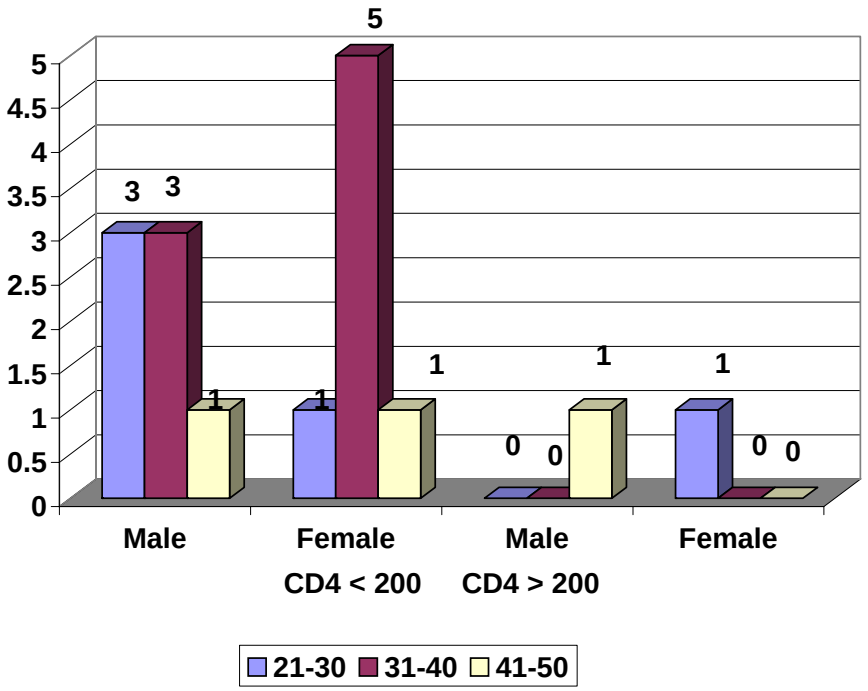


Table - 11

Distribution of cases and controls with respect to biochemical Parameters

Biochemical parameter	Cases		Controls		P value
	Mean	SD	Mean	SD	
Bl.sugar	85.77	7.07	87.89	7.79	0.3045
Bl.urea	29.33	8.89	24.42	4.03	0.0012
Sr.creatinine	0.99	0.39	0.85	0.11	0.0146
Sr.Na+	138.88	3.39	140.56	3.35	0.0666
Sr K+	4.10	0.47	4.21	`	0.2594

There is statistically significant difference between cases and controls with respect to blood urea and Sr.creatinine which can be attribute to the renal involvement. But with respect to Bl.sugar, Sr.sodium, Sr.pottassium, there is no statistically significant difference between cases and controls.

Table - 12

Microalbuminuria in relation to CD4 counts

CD4 count	**Microalbuminuria**	**Normal**
CD4 < 200 (Group A)	14	16
CD4 > 200 (Group B)	2	28

This table shows statistically significant increase in the prevalence of microalbuminuria with decrease in the CD4 count. Out of 30 cases in group A who had CD4 count <200, microalbuminuria is seen in 14 cases . In group B who had CD4 count >200, microalbuminuria is seen only in 2 cases.

Table -13

Urine albumin / creatinine ratio among case and controls

	Cases		Controls	
	Mean	SD	Mean	SD
Urine Al/cr Ratio	39.6	51.89	10.14	1.64

P < 0.000001

The mean urine albumin / creatinine ratio is 39.6 mg/g (SD 51.89) in cases and 10.14 mg/g (SD 1.64) in controls . P value is < 0.000001, it indicates statistically higher significant difference between cases and controls with respect to urine albumin creatinine ratio.

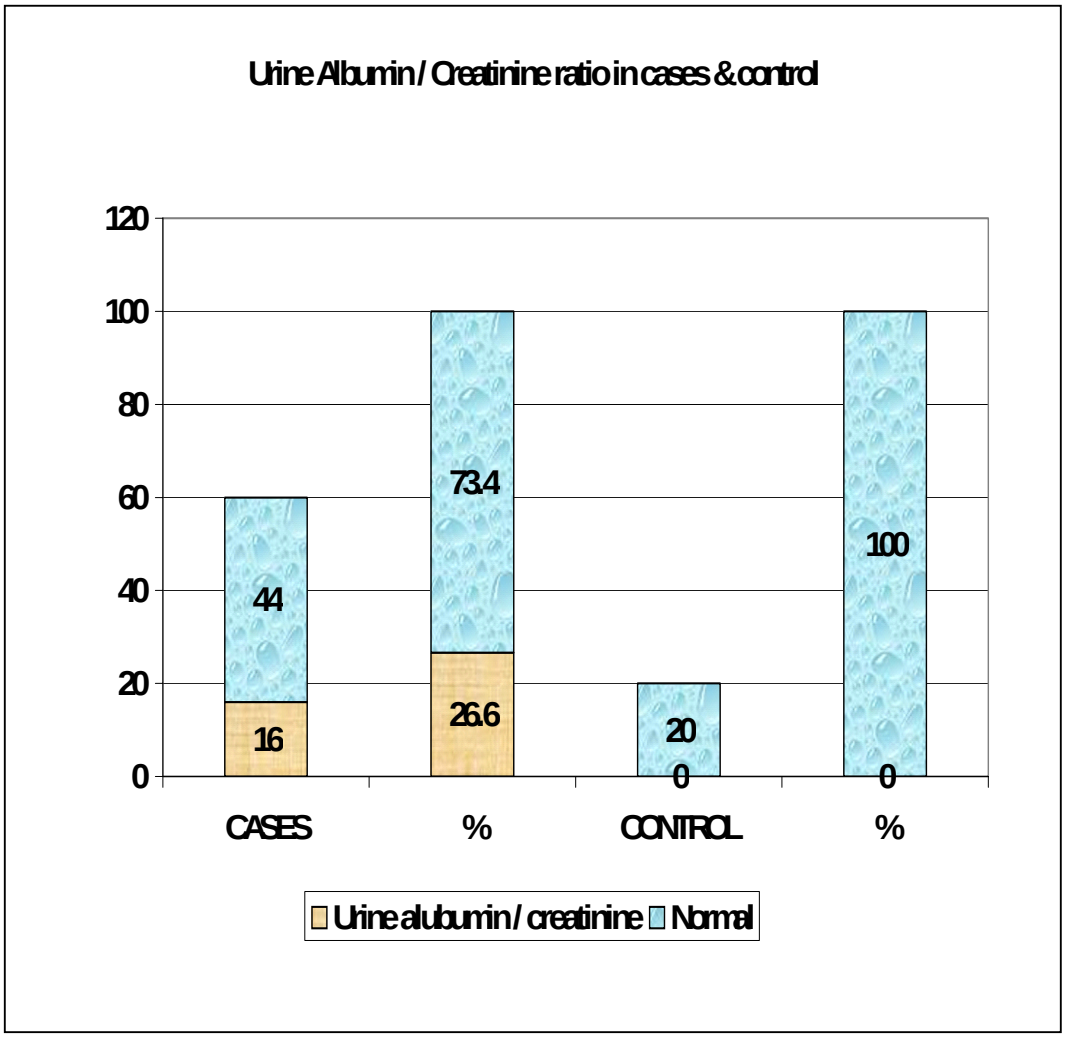

Urine Albumin / Creatinine ratio in cases & control
120
100
80
60
40
20
0
44
16
73.4
26.6
20
0
100
0
CASES
%
CONTROL
%
Urine alubumin / creatinine
Normal

Table -14

Distribution of cases and controls in relation to 24 hours urine protein

	Cases		Controls	
	Mean	**SD**	**Mean**	**SD**
24 hours urine protein	184.50	129.69	93.05	10.12

P < 0.000001

The mean urine 24 hours protein is 184.50 mg/day (SD 129.69) in cases and 93.05 mg/day (SD 10.12) in controls. P value is < 0.000001, it indicates there is a statistically higher significant difference between cases and controls with respect to 24 hours urine protein.

Table – 15

Overt Proteinuria in cases with respect to CD4 count

CD4 count	Microalbuminuria	Overt Proteinuria
CD4 < 200	14	6
CD4 > 200	2	1

This table shows that in group A with CD4 count < 200, microalbuminuria occurs in 14 cases, of which 6 patients (42.8 %) had overt proteinuria. Where as in group B with CD4 > 200, microalbuminuria occurs in 2 cases, of which 1 patient had overt proteinuria.

DISCUSSION

HIV infection is the pandemic of modern society. Renal disorders are encountered at all stages of HIV infection.[3]

Microalbuminuria is the earliest marker of the renal involvement, microalbuminuria is seen in approximately 20% of untreated HIV infected patients.[34]

Winston JA et al [43] noted HIVAN has become the third leading cause of ESRD among African Americans aged 20-64 years.

Luke DR et al, [45] study observed that micro albumin levels were not correlated with age, sex. In our study also, microalbuminuria levels were not affected by age and sex.

The prevalence of microalbuminuria in HIV and AIDS patients differ in various studies. Luke DR et al,[45] study noted 19.4% of patients had abnormal levels of microalbuminuria. Kimmel PL et al ,[47] study showed microalbuminuria in 20 to 30% of HIV patients .

In our study, the prevalence of microalbuminuria was found to be 26.6% . The mean microalbuminuria value was 31.14 mg/day (SD 34.34) among cases and 2.93 mg/day (SD 2.68) among controls. P value is < 0.000001. It indicates statistically highly significant difference in cases and controls with respect to microalbuminuria.

Kimmel PL et al, Umana WO et al [48] noticed that, the prevalence of an increased urinary albumin / creatinine ratio was 29.8% in the HIV infected patients. In Buch [46] HW et al study, the prevalence rate was 13.4% . In our study the urinary albumin / creatinine ratio was 26.6% in HIV and AIDS patients. The mean urine albumin / creatinine ratio is 39.6 mg/g (SD 51.89) in cases and 10.14 mg/g (SD 1.64) in controls . P value is < 0.000001, it indicates statistically highly significant difference in cases and controls with respect to urine albumin / creatinine ratio.

Several studies have suggested that abnormality of protein excretion, without frank nephrotic syndrome is common in HIV infected populations. In Agaba EI et al,[49] proteinuria was detected in 25.3% of HIV patients. In Cravley ST et al,[50] study the prevalence of asymptomatic proteinuria was 14% and the presence of proteinuria was not correlated with viral load .

Varma PP et al,[51] study showed overt proteinuria was detected in 17.6% of HIV patients. In Gardner et al,[52] overt proteinuria was present in 11.2% of HIV seropositive women. In our study, 11.6% of HIV seropositive patients had Overt proteinuria .

In our study, 7 patients had overt proteinuria out of 16 microalbuminuria patients (43.75%). Luke DR et al,[45] study showed overt proteinuria in 7 out of 14 microalbuminuria patients(50%).

Various studies show that there is a strong correlation between CD4 count and microalbuminuria level. Szczech LA et al [41], Busch HW et al [46] and Atta MG et al[53] studies also confirmed that, microalbuminuria is seen in exclusively with CD4 count below 200/mm^3.

In our study , 16 out of 60 patients had elevated urinary levels of micro albumin, of which 14 patients found to have CD4 count <200/mm^3.

In our study revealed abnormalities of Sr.Creatinine in 4 male and 4 female patients. Of which 7 patients who had elevated creatinine were found to have CD4 count < 200/mm^3.

Though there was biochemical evidence of mild renal failure, they did not reveal any symptomatology related to glomerular or interstitial involvement. Thus this study revealed that HIV infected and AIDS individuals may have asymptomatic renal involvement.

No electrolyte abnormalities were seen in our study. How ever the review of literature showed that the commonest fluid and electrolyte abnormalities seen in HIV and AIDS cases is hyponatremia.

Behar DM et al [54] and Winston JA et al,[43] studies show that type of renal involvement varied in different geographic regions. For instance, in US there was remarkable differences for the geographic distribution of HIVAN. In this group, patients with heavy proteinuria developed progressive renal disease. South Indian population, have some similarities as black population in renal involvement.

Gardner, Lytt I et al,[52] showed proteinuria or elevated sr.creatinine in HIV infected women were associated with an increased risk of death after controlling the other risk factors. Hence HIV infected patients have to be closely monitored for their renal function and for microalbuminuria.

This will help to identify

a) The triggering factor
b) The progression of renal involvement
c) To minimize the renal complication by early intervention.

SUMMARY

The present study was aimed to study the microalbuminuria level in HIV seropositive patients, and also to find out its association with CD4 counts. With rigid criteria 60 HIV seropositive cases and 20 controls were selected. The controls were matched for age and sex compared to cases. There were 31 males and 29 females in the case group and 10 males and 10 females in control group.

This study projects high prevalence of microalbuminuria (26.6%) in HIV and AIDS patients. The mean microalbuminuria value was 31.14 mg/day (SD34.34) among the cases and 2.93 mg/day (SD 2.68) among the controls .

This study showed the urinary albumin/creatinine ratio was 26.6% in HIV and AIDS patients . The mean albumin/creatinine ratio is 39.6 mg/g in cases and 10.14 mg/g in controls. In our study overt proteinuria present in 11.6% of HIV seropositive patients.

Microalbuminuria levels were specifically co related with CD4 counts. In this study noted 14 patients out of 16 microalbuminuria cases found to have CD4 count <200/mm^3.

The present study revealed abnormalities of Sr.creatinine in 8 patients , of which 7 patients were found to have CD4 count <200/mm3.

Therefore urinary screening for microalbuminuria in HIV and AIDS patients may help to identify renal involvement and to minimize the renal complication by early intervention and avoidance of nephro toxic drugs in management.

CONCLUSION

- Both sexs are equally affected. Microalbuminuria levels had no cor - relation with the gender and age.

- Microalbuminuria was significantly elevated in HIV and AIDS cases, it was seen in 26.6% of cases . The mean microalbuminuria value was 31.14 mg/day in cases and 2.93 mg/day in controls.

- The prevalence of urinary albumin / creatinine ratio was 26.6% in HIV and AIDS patients. The mean urine albumin / creatinine ratio is 39.6 mg/g in cases and 10.14 mg/g in controls .

- The microalbuminuria levels were specifically correlated with CD4 counts. 14 out of 16 HIV and AIDS patients were found to have CD4 count <200/mm3.

- Sr.creatinine level is elevated in 8 patients, of which 7 of the patients with elevated creatinine were found to have CD4 count <200/mm^3.

- Overt proteinuria is present in 11.6 % of HIV seropositive patients.

- Sr. sodium, potassium are not altered in the study groups.

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PROFORMA

MICROALBUMINURIA IN HIV & AIDS PATIENTS

NAME AGE SEX OCCUPATION

ADDRESS IP.NO :

COMPLAINTS

HISTORY OF PATIENTS ILLNESS:

- ☐ Loss of appetite & weight
- ☐ Leg swelling
- ☐ Diarrhea
- ☐ Facial puffiness
- ☐ Vomiting
- ☐ Hiccough
- ☐ Fever
- ☐ Haematuria
- ☐ Cough with expectoration
- ☐ Head ache
- ☐ Frequency of micturition
- ☐ Chest pain
- ☐ Oliguria

HISTORY OF PAST ILLNESS:-

☐ Old PT & treatment with ATT ☐DM ☐ Renal disease

☐ IHD ☐ CCF ☐Jaundice ☐Blood transfusion

☐ Any other (specify)

PERSONAL H/o:-

- ☐ Smoking
- ☐ Alcholic
- ☐ Sexual promiscuity
- ☐ Marital status
- ☐ Drug addition/abuse

GENERAL EXAMINATION:-

Height Weight

PR:- BP:-

☐ Aneamia ☐ Jaundice ☐ Clubbing

☐ Paedal edema ☐ Lymphadenopathy

SYSTEMATIC EXAMINATION:-

RS

CVS

ABDOMEN

CNS

INVESTIGATION:-

URINE - Albumin
- Sugar
- Deposit

Bl.Sugar
Bl.urea
Bl.Creatinine

Sr.Eletrolytes Na^+
Cl^-

Urine albumin & creatitinine ratio

MICRO ALBUMIN

24 hrs urinary protein

Sero positivity HIV 1 ☐Reactive CD4 count

HIV 2 ☐Non reactive DC,TC,HB%

ECG

USG Abdomen.

MASTER CHART

S.No	Age	Sex	CD4	CD8	CD4/CD8 ratio	Sugar	Urea	Creatinine	NA+	CL-	Micro albumin	Urine Al/cr ratio	24 hrs urine protein
1	45	F	586	1095	0.54	80	18	0.7	138	3.8	2.5	10.5	125
2	40	M	339	586	0.58	92	18	0.7	136	3.9	1.8	9.2	130
3	35	F	792	1215	0.65	76	28	0.6	138	3.3	6	8.3	50
4	31	M	145	476	0.30	86	24	0.8	140	4.2	28	19	256
5	28	F	964	630	1.53	95	23	0.7	138	4.5	2.5	16.5	136
6	25	M	64	1029	0.06	82	38	1.2	138	4.3	44	76	345
7	35	F	40	343	0.12	78	40	1.4	145	3.8	48	62	280
8	37	F	256	585	0.16	80	22	0.6	140	4.6	18	22	126
9	42	M	438	1523	0.28	88	21	0.7	136	4.5	14	11	125
10	30	M	172	560	0.31	90	31	0.7	143	5.2	28	18	150
11	34	F	198	720	0.3	76	27	0.6	136	3.8	26	20	172
12	31	F	195	>2000	<0.10	70	32	0.8	136	3.8	46	68	260
13	38	F	204	1127	0.18	76	24	0.7	139	3.2	10	16	88
14	30	F	757	1388	0.55	82	26	0.8	136	4.2	13	12	102
15	37	M	253	1895	0.13	80	28	0.9	138	4.6	12	18	60
16	29	F	374	>2000	<0.19	92	27	0.7	135	4.8	26	24	116
17	31	M	276	>2000	<0.14	90	38	0.8	140	3.8	13	9.8	182
18	36	F	53	980	0.05	87	48	2.1	148	4.6	118	202	240
19	21	F	783	837	0.94	83	20	0.6	138	4.2	6	14	96
20	30	M	62	421	0.15	80	33	0.8	140	3.8	16	20	80
21	28	M	63	439	0.14	89	26	0.9	138	4.5	28	18	142
22	35	M	117	720	0.16	94	33	0.7	140	4.4	62	89	212
23	41	M	16	570	0.03	102	52	1.9	142	3.6	137	143	495
24	40	M	83	444	0.19	78	32	1	140	4.8	12	18	120
25	27	F	553	1760	0.3	84	26	0.9	135	5.1	8	12	80
26	32	M	123	656	0.19	90	25	0.8	138	3.9	28	13	96
27	30	F	195	412	0.47	78	28	0.9	136	4.1	4	15.6	108
28	30	F	183	1315	0.13	92	26	0.9	138	4	68	110	258
29	33	F	182	918	0.19	80	22	0.6	139	3.8	22	18	172

30	30	F	112	566	0.22	86	38	0.9	136	3.5	15	21	135
31	43	F	196	786	0.25	90	16	0.7	140	3.6	18	9.1	112
32	38	M	562	790	0.71	84	20	0.9	136	4.1	4	17	128
33	35	M	1046	826	1.27	76	28	1.1	135	3.9	1.7	8	88
34	35	F	18	225	0.08	87	48	2.2	138	3.6	110	115	700
35	38	M	579	1179	0.49	91	32	1	136	3.6	19	23	186
36	45	F	42	1076	0.04	98	28	0.8	139	3.8	24	28	210
37	50	F	104	379	0.27	105	18	1.1	138	4	22	16	156
38	35	M	60	463	0.13	88	48	1,8	138	4.4	160	299	640
39	30	M	198	407	0.49	92	20	0.9	135	4	14	20	168
40	34	M	147	426	0.35	80	26	0.8	136	4.2	5	10	112
41	34	M	602	1366	0.44	76	22	1.2	136	4.5	6	18	128
42	32	M	356	815	0.44	88	32	1	141	3.6	8	14	112
43	21	M	47	922	0.05	82	22	0.8	143	4.4	44	36	156
44	36	M	394	>2000	<0.35	85	28	0.8	138	4.2	6	16	190
45	37	M	212	634	0.33	81	26	0.9	148	4.3	18	26	126
46	44	F	45	295	0.15	79	26	0.8	138	3.2	38	52	186
47	35	M	292	788	0.37	92	18	1.2	142	3.5	20	24	192
48	33	M	695	1383	0.50	88	23	0.9	138	3.9	26	11	148
49	30	M	171	1673	0.1O	93	42	1.5	138	3.8	48	62	216
50	23	M	291	864	0.34	80	32	0.8	132	4.6	16	24	176
51	37	M	29	500	0.06	86	38	1.9	142	5.2	84	122	300
52	30	F	252	1191	0.21	91	24	0.9	146	4.2	26	19	165
53	28	F	32	500	0.06	79	52	1.7	143	4.8	58	116	456
54	30	M	721	1290	0.56	80	23	0.6	143	3.8	8	12	86
55	27	F	311	978	0.32	94	28	1.1	134	3.6	12	18	134
56	29	F	309	>2000	<0.15	80	44	1.9	145	4.5	94	64	325
57	27	F	528	1841	0.28	96	24	0.9	136	4.5	10	14	80
58	43	M	233	1318	0.18	92	36	1.4	144	3.9	74	40	215
59	32	F	40	687	0.06	87	38	1.3	137	3.6	18	20	155
60	32	F	224	490	0.5	90	24	1.2	138	4	14	9	75

CONTROLS

S.NO	AGE	SEX	SUGAR	UREA	CREATININE	NA+	CL-	MICRO ALBUMIN	URINE AL/CR RATIO	24 HRS URINE PROTEIN
1	33	M	88	22	0.8	138	4.3	1.25	10.5	78
2	28	M	90	24	0.9	136	3.8	<2.25	9.85	92
3	38	F	78	32	0.9	144	4.5	<2.25	11	86
4	42	F	95	28	0.7	139	4.6	1.85	9.8	96
5	26	M	98	26	0.9	146	4.1	2.5	12.6	102
6	36	M	79	20	0.8	138	3.6	2.5	11.7	90
7	44	M	82	28	0.9	140	4.1	12	<13	112
8	35	F	86	26	1	142	4.5	2.5	10.5	82
9	28	F	93	24	0.7	138	4.3	1.25	11.5	90
10	22	M	80	22	0.9	136	3.8	2.5	8	88
11	26	F	92	30	1.1	148	4.7	8	11.2	106
12	31	F	78	26	0.7	143	3.9	2.5	10.1	98
13	26	M	100	28	0.9	139	4.4	4	11.5	80
14	39	M	94	20	1	141	4.2	1.05	8.2	92
15	25	F	99	22	0.8	138	4.6	2.5	10.2	88
16	30	F	87	18	0.9	140	4	1.05	10.8	92
17	36	M	83	28	0.8	139	4.3	2.5	6	102
18	40	F	80	18	0.7	145	4.1	2	8	82
19	32	M	92	22	0.8	136	3.9	1.25	11	112
20	26	F	97	28	1.1	138	3.7	2.5	12	90